OVERVIEW OF LINDANE RISK ASSESSMENT

August 16, 2001

Introduction

This document provides an overview of EPA's human health, environmental fate and transport, and ecological risk findings for the pesticide Lindane as presented fully in the documents, "Revised Human Health Risk Assessment for Lindane," dated July 31, 2001 and "EFED (Environmental Fate and Effects Division) RED Chapter," dated August 1, 2001. The purpose of this overview is to assist the reader by identifying the key features and findings of these risk assessments in order to better understand the conclusions reached in the assessments. This overview format was developed in response to comments and requests from the public which indicated that Agency risk assessments were difficult to understand, that they were too lengthy, and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

The Food Quality Protection Act (FQPA) requires that the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The reason EPA considers other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. The Agency has not performed a cumulative risk assessment as part of this reregistration review of lindane because it has not determined there are any other chemical substances that have a common mechanism of toxicity. If the Agency identifies other substances that share a common mechanism of toxicity with lindane, then a cumulative risk assessment will be conducted that includes lindane once the final framework the Agency will use for conducting cumulative risk assessments is available. Further, the Agency is in the process of developing criteria for characterizing and testing endocrine disrupting chemicals, in accordance with FQPA. EPA plans to implement an Endocrine Disruptor Screening Program at a later date; lindane will be reevaluated at that time and additional testing may be required.

The risk assessments for lindane and additional supporting documents are posted on EPA's Internet website (http://www.epa.gov/pesticides/lindane.htm) and are available in the Pesticide Docket for public viewing. The Agency plans to discuss the risk assessments, identify risks of concern, and solicit input on risk mitigation strategies (if needed) with stakeholders (growers, extension offices, states, tribes, commodity groups, the general public, and other Federal agencies). This feedback will be used to complete the Reregistration Eligibility Decision

(RED) document, which describes the Agency's risk management decisions for lindane. Prior to finalizing the reregistration decision, the Agency will conduct a close-out conference call with interested stakeholders to describe the regulatory decisions that will be presented in the RED.

Use Profile

Manufacturer/Technical Registrant: INQUINOSA Internacional, S.A. (Industries Quimica de Nordouesta SA). Sole member of the Centre Internationale d'Etudes du Lindane (CIEL, the Lindane task force).

- **Type of Pesticide:** Insecticide.
- **Target pests:** Seed corn beetles, seed corn maggots, white grubs, and wireworms.
- **Crops/use sites:** Registered for use on the following crops/sites: (for seed treatment only), barley, broccoli, Brussels sprouts, cabbage, cauliflower, corn, lettuce, oats, radishes, rye, sorghum, spinach, and wheat. The RED will also consider the pending registration on canola (seed treatment only as well).
- **Formulations:** Crystalline, Dust, Emulsifiable concentrate, Flowable concentrate, Liquid-ready to use, Wettable powder, Wettable powder/dust.
- **Methods of Application:** Liquid seed treater; Planter/seed box; Seed treater; Slurry-type seed treater.
- **Use Rates:** 0.031 to 0.125 lbs ai/100 lbs of seed. (The registrant has applied for a new use on canola. If approved, the maximum application rate on canola would be 1.5 lbs ai/100 lbs seed.)
- **Annual Poundage:** Up to 200,000 lbs/year.
- **Other Registrants:** AGSCO, INC., Prentiss Inc., WILBUR-ELLIS COMPANY, Gustafason, Platt Chemical, Trace Chemicals, Inc., Wilfarm LLC., ORCAL, INC., Drexel Company, and ZENECA Corp.
- **Classification:** General use.
- **Timing**: Used as a pre-plant seed treatment only.

Human Health Risk Assessment

Acute Toxicity

- Lindane has been placed in Acute Toxicity Category II for exposures by the oral and dermal routes and in Acute Toxicity Category III for eye irritation.

Acute Dietary (Food) Risk

Acute dietary risk is calculated considering what is eaten in one day. Dietary exposure that is less than 100% of the acute Population Adjusted Dose (aPAD) (the dose at which an individual could be exposed on any given day that would not be expected to result in adverse health effects) does not exceed the Agency's risk concern. The aPAD is the acute Reference Dose (RfD) adjusted for the FQPA Safety Factor.

An acute dietary analysis was conducted using anticipated residues for all commodities supported for reregistration including a proposed new use on canola. The dietary assessment, which is a Tier 3 probabilistic assessment based on the Dietary Exposure Evaluation Model (DEEM™), was conducted using percent crop treated and total radioactive residues (TRRs) from plant metabolism studies and from poultry and ruminant metabolism studies. A processing study for canola found no detectable lindane residues in canola oil, therefore, one half the limit of quantitation (½ LOQ) was used as the DEEM™ adjustment factor. DEEM™ default adjustment factors were used for all other concentration factors.

- The acute dietary (food) risk estimate is not of concern for any population subgroups at the 99.9th percentile. The highest dietary risk estimate is 17 % of the aPAD for the population subgroup All Infants. For the U.S. population, the estimate is 7% of the aPAD.

- The acute dietary endpoint was derived from an acute neurotoxicity study in rats. The No Observable Adverse Effect Level (NOAEL) for neurotoxic effects was 6 mg/kg for females and the Lowest Observable Adverse Effect Level (LOAEL) was 20 mg/kg based on increased forelimb grip strength and decreased grooming behavior and motor activity.

- An uncertainty factor (UF) of 300 was applied to account for inter-species extrapolation (10X), intra-species variation (10X), and the FQPA safety factor (3X).

- An FQPA safety factor of 3X is required for lindane since there is evidence of increased susceptibility of the young demonstrated in both the developmental neurotoxicity study (quantitative) and the 2-generation reproduction study in rats (qualitative).

- The FQPA safety factor was reduced to 3X because: 1) the toxicology database is complete; 2) available data provide no indication of increased susceptibility in rats from *in utero* exposure to lindane; 3) the offspring effects seen in the developmental neurotoxicity study were the same as those seen in the two-generation reproduction study (no additional functional or morphological hazards to the nervous system were noted); 4) adequate data (surrogate and/or modeling outputs) are available to assess food exposure and to provide a screening level drinking water exposure assessment; 5) the developmental toxicity study in rabbits, shows no developmental effects at the maternally toxic dose; 6) a developmental neurotoxicity (DNT) study has already been submitted; and 7) there are no residential uses.

- Therefore, the aPAD is 0.02 mg/kg/day. (NOAEL of 6 mg/kg/day divided by 300 (Uncertainty Factor of 100 and FQPA safety factor of 3).

Chronic Dietary (Food) Risk

Chronic dietary risk is calculated by using the average consumption value for food and average residue values on those foods over a 70-year lifetime. A risk estimate that is less than 100% of the chronic Population Adjusted Dose (cPAD) does not exceed the Agency's level of concern. The cPAD is the chronic Reference Dose (cRfD) adjusted for the FQPA Safety Factor. The RfD is the dose at which an individual could be exposed over the course of a lifetime with no adverse health effects.

The chronic dietary analysis was conducted using anticipated residues for all commodities supported for reregistration including a proposed new use on canola. The chronic dietary assessment was based on the Dietary Exposure Evaluation Model (DEEM™) using percent crop treated and total radioactive residues (TRRs) from plant metabolism studies and from poultry and ruminant metabolism studies. A processing study for canola found no detectable lindane residues in canola oil, therefore, ½ LOQ was used as the DEEM™ adjustment factor. DEEM™ default adjustment factors were used for all other concentration factors.

- Chronic dietary risk from food is not of concern. For the most highly exposed sub-population, Children 1-6 years, exposure is 11% of the cPAD; while the exposure for the U.S. population is 3% of the cPAD.

- The chronic dietary endpoint is derived from a chronic toxicity/oncogenicity study in rats. The systemic toxicity NOAEL is 0.47 mg/kg/day based on increased liver and spleen weights and decreased platelets. The LOAEL is 4.81 mg/kg/day.

- An uncertainty factor (UF) of 300 was applied to account for inter-species extrapolation

(10X), intra-species variation (10X), and the FQPA safety factor (3X).

- The FQPA safety factor of 3X was retained for chronic dietary exposures for the reasons described above in the acute dietary discussion.

- Therefore, the cPAD was determined to be 0.0016 mg/kg/day [NOAEL of 0.0047 mg/kg/day divided by 300 (UF of 100 multiplied by the FQPA safety factor of 3).]

Subpopulation Dietary Assessment

Lindane does not occur naturally in the environment. Once released into the environment, lindane can partition into all environmental media. Because of long-range atmospheric transport, lindane has been detected in air, surface water, groundwater, sediment, soil, ice, snowpack, fish, wildlife, and humans. The Arctic is considered a "sink" for persistent organic pollutants such as lindane. Once in the Arctic, lindane bio-accumulates in the food chain due to its high lipid solubility. Lindane is bio-concentrated rapidly in microrganisms, invertebrates, fish, birds and mammals. However, bio-transformation and elimination are relatively rapid when exposure is discontinued.

The indigenous people of the US Arctic region (Alaska) rely heavily on subsistence diets as their food source. Because Lindane concentrates in fish and game, the Agency performed a supplementary dietary risk and exposure assessment to determine risk to indigenous people from worldwide use and manufacture of lindane. Although the data set available to support this analysis was limited, the results did not exceed the Agency's level of concern. Chronic dietary risk based on traditional foods is not of concern. For the most highly exposed sub-population, Children 1-6 years, the subsistence diet results in Lindane exposure at 44% of the cPAD; while for the adult population the subsistence diet is 6% of the cPAD. An acute dietary assessment (aPAD) is not possible at this time because the Agency does not have the information on a typical day's diet of indigenous people. Chronic assessments were done based on average residues in diet.

Cancer Dietary (Food) Risk

No dietary cancer risks for lindane were estimated. A mouse cancer study was submitted on December 31, 2000. Additional histopathology information was submitted August 3, 2001. This information is currently being reviewed. The Agency will include these results in the revised risk assessment. The carcinogenic potential of lindane will be reassessed after the Agency completes the review of the mouse carcinogenicity study and these supplemental data.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. To determine the maximum allowable contribution of treated water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by food, then determines a "drinking water level of comparison" (DWLOC) to determine whether modeled or monitoring concentrations exceed this level. DWLOCs were calculated based on the dietary exposure and default body weights and water consumption figures.

The Agency uses the DWLOC as a surrogate to capture risk associated with exposure from pesticides in drinking water. The DWLOC is the concentration of a chemical in drinking water that would be acceptable as an upper limit considering total aggregate exposure to that chemical from food, water, and residential sources. Risks from drinking water are assessed by comparing the DWLOCs to the estimated environmental concentrations (EECs) in surface water and groundwater. Drinking water modeling is considered to be an unrefined assessment and provides high-end or conservative estimates so modeling tends to overestimate risk.

Surface water estimated environmental concentrations (EECs) resulting from lindane seed treatment use were predicted with the Tier 1 assessment model, GENEEC. Groundwater EECs were estimated using SCI-GROW

Acute Drinking Water. The highest EECs for Lindane in surface water (0.67 ppb, from GENEEC) and in groundwater (0.011 ppb, from SCI-GROW) are less than the acute DWLOCs for all sub-populations (lowest acute DWLOC = 170 ppb) indicating that acute aggregate exposure to lindane in food and water only does not exceed the Agency's level of concern.

Chronic Drinking Water. The chronic EECs for Lindane in surface water (0.16 ppb, from GENEEC) and in groundwater (0.011 ppb, from SCI-GROW) are less than the chronic DWLOC (14 ppb), indicating that chronic exposure to lindane in food and water only is less than the Agency's level of concern.

In the U.S. EPA STORET data base, 720 detections of lindane in ground water were reported between the years 1968 and 1995, in nearly all regions of the country, with especially high numbers of detections in the South and West. For these 720 detections, the median and mean concentrations were 0.01 and 11 ppb, respectively. For surface waters, 8775 detections were reported with median and mean concentrations of 0.005 and 0.18 ppb. In the USGS NAWQA study, lindane was detected in 2.58% of surface water samples (0.67% at levels greater than 0.05 ppb, maximum concentration reported was 0.13 ppb). For groundwater, USGS NAWQA reported a detection frequency of 0.1 % (0.07% at levels greater than 0.01 ppb, maximum concentration reported was 0.032 ppb). Although these long-term monitoring programs have

detected lindane in various water bodies, the Agency determined that these data are not suitable for risk assessment, because there is no correlation of monitoring with actual lindane use. Therefore, these data are presented here solely for informational purposes.

Residential Risk

There are no residential or other non-agricultural FIFRA uses of Lindane.

Aggregate Risk

The aggregate risk assessment for lindane examines the combined risk from exposure through food and drinking water only since there are no residential or other non-agricultural uses of Lindane. Therefore, the DWLOC was calculated based only on dietary exposures. As noted above neither acute nor chronic, surface water or ground water EECs exceed the DWLOC and therefore do not exceed the Agency's level of concern.

Occupational Risk

The Agency assessed 5 scenarios for worker exposure. Workers can be exposed to a lindane through (1) on farm through mixing/loading/planting dry seed treatment, (2) on farm loading of commercially treated seeds, (3) planting of commercially treated seeds, (4) commercial mixer/loader/applicator using liquid treating formulation, and (5) handling treated seed during commercial seed treatment. Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to NOAEL taken from animal studies. Generally, MOEs greater than100 do not exceed the Agency's level of concern. For Lindane, a dermal absorption factor of 10% was used to account for differences in absorption between the oral and dermal routes.

- Workers are exposed to Lindane via both the dermal and inhalation routes; therefore EPA selected toxicological endpoints appropriate to these routes of exposure.

- The dermal endpoint is derived from a rat oral developmental neurotoxicity study. A NOAEL 1.2 mg/kg/day was established based on reduced pup survival, decreased body weight and body weight gains during lactation, increased motor activity, and decreased motor activity habituation. A 10% dermal absorption factor was used.

- The inhalation endpoint is derived from a 90-day rat inhalation study. The inhalation NOAEL was established at 0.13 mg/kg/day based on clinical signs (diarrhea, piloerection), increased kidney weights, and bone marrow effects.

- An uncertainty factor of 100 was applied (10X for inter-species extrapolation and 10X for intra-species variation) to calculate risks for exposure from both the inhalation and dermal

routes. An MOE of 100 or greater is not of concern.

- Because the endpoints for dermal and inhalation are different, exposures from different routes are not combined and separate MOEs are calculated.

- For the worker risk assessment, EPA assumes that "on farm" workers wear a single layer of clothing (long pants and long sleeve shirt) and gloves. EPA assumes that commercial seed treatment workers wear a second layer of clothing (coveralls). The Agency did not calculate worker risks with closed mixing loading systems (engineering controls).

- *Existing seed treatment uses*. There is one dermal MOE of 19 for "on farm" mixing-loading-planting activities which exceeds the Agency's level of concern. All other short and intermediate term dermal and inhalation MOEs range from 98 to 43,000 and do not exceed the Agency's level of concern.

- *Canola Use*. The canola seed treatment rate (1.5 lbs. ai/100 lbs of seed) would be approximately 40 times greater than other seed treatment uses of Lindane assessed by the Agency. Mixing, loading, and application of the liquid formulation for commercial seed treatment would result in dermal MOEs ranging from 5.3 for large facilities to 40 for small/medium facilities and inhalation MOEs ranging from 2.6 for large facilities to 20 for small/medium facilities which exceed the Agency's level of concern. Commercial handler MOEs would range from 150 for large facilities to1200 for small/medium facilities while inhalation MOEs would range from 20 to 150 for large and small/medium facilities, respectively. Use of a respirator would improve the inhalation MOEs by a factor of 10X.

Post-Application Occupational Risk

The Agency has determined that once seeds treated with Lindane have been planted in the ground, any potential post planting exposure or risk to individuals is negligible.

Ecological Risk

To estimate potential ecological risk, EPA integrates the results of exposure and ecotoxicity studies using the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic, for various wildlife species. RQs are then compared to levels of concern (LOCs). Generally, the higher the RQ, the greater the potential risk.

Environmental Fate and Transport

Lindane is persistent and moderately mobile. It is resistant to photolysis and hydrolysis (except at high pH), and degrades very slowly by microbial actions. Lindane bioconcentrates,

but in the absence of additional sources of Lindane, it purges rapidly.

Lindane is transported through the environment by both hydrologic and atmospheric means. Lindane has often been detected in surface and ground water, and lindane and its isomers have been detected in areas of non use (e.g., the Arctic), indicating global atmospheric transport may occur. The source of these lindane detections is unclear but may be the result of a combination of lindane's past widespread use and its extreme persistence. Currently, U.S. uses of lindane are restricted to (agricultural) seed treatments at relatively low application rates.

Nontarget Terrestrial Risk

- Seed treatment uses present acute and chronic risk to birds and mammals. In addition, there is a possibility of acute risk to small mammals with high metabolic rates that dig and cache seeds. Chronic risk to these species may be greater during breeding season due to high seed consumption over time and the persistence of the compound in soil.

- There is acute risk to songbirds and other similar seed eating avian species; however, some studies have shown that birds when given a choice of seeds will preferentially eat seeds not treated with lindane.

- Lindane is highly toxic (0.2 to 0.56 ug/bee) to honeybees. However, because of the nature of the seed treatment use, EPA assumes low risk to flying insects. Beneficial soil dwelling insects may be at some risk.

Risks to Endangered Species

Endangered birds and especially small mammals that eat a large daily proportion of seeds may be at risk from the proposed canola seed treatment. Endangered freshwater fish and invertebrates may also be at acute risk. Also, exposed endangered birds, mammals and possibly fish may be jeopardized due to the endocrine disrupting properties of lindane combined with already limited population sizes and/or losses in critical habitat.

Nontarget Aquatic Risk

Risk is based on the assumption that 100% of the lindane from the seed treatment migrates to surface water after planting. However, some lindane from seed treatment is expected to remain with the seed/plant, or in the soil or volatilize.

- At current application rates used on major crops, acute high risk and restricted use levels of concern are exceeded for both freshwater and estuarine/marine organisms.

- No chronic LOC's are exceeded for freshwater fish and invertebrates while chronic risk to estuarine/marine fish could not be assessed due to a lack of toxicity data.